

cell or nerve cell-protective agents comprising ginsenoside Rb<sub>1</sub>"), ginsenoside Rb<sub>1</sub> of the present invention, when administered to rats with permanent MCA occlusion (body weight about 300 g) in the doses of 6  $\mu$ g and 60  $\mu$ g/day, caused reduction of the cerebral infarction area and ameliorated ischemia-induced place navigation disability (cerebrovascular dementia). Furthermore, ginsenoside Rb<sub>1</sub> of the present invention, in its equivalent doses, promotes cerebrovascular regeneration and/or reconstruction in the non-infarcted ischemic penumbra of the rats with permanent MCA occlusion, and significantly inhibits the secondary lesion of the thalamus (secondary thalamic degeneration) in addition to reducing cerebrocortical infarct lesion (the primary ischemic lesion). Intravenous administration of ginsenoside Rb<sub>1</sub>, in the dose of 60  $\mu$ g/day or 12  $\mu$ g/day, to rats with spinal cord (lower thoracic spinal cord) injuries significantly ameliorates paralysis or paraplegia.

Based on these experimental results, the dose range of ginsenoside Rb<sub>1</sub> to human patients with cerebral apoplexy (body weight 60 kg) is calculated as 1.2 mg - 12 mg/day. Consequently, daily doses of the pharmaceutical composition of the present invention to human patients with cerebral apoplexy or spinal cord injuries is, although depending on individual differences and on the severity of diseases among patients, 0.1 mg or more, preferably 1 mg or more, more preferably 10 mg or more. However, since required dose amount per body weight is, generally,

decreased as the body weight of animals increases, a dose of 1/10 or less of this amount is thought to exhibit sufficient effects on human. When ginsenoside  $Rb_1$  is used for prevention, therapy or treatment of diseases other than central nervous system (CNS) diseases, it is preferable to select the equivalent dose of the above, or doses of 1/10 to 1/100,000 thereof. Since the pharmaceutical composition of the present invention has less adverse effect, it can be administered considerably in large amount as an upper limit of dosage, and the upper limit of dosage is 1 g or less/day, preferably 0.1 g or less/day.

The method for administration of the pharmaceutical compositions of the present invention is intravascular administration, preferably intravenous administration and the amount of administration described above can be administered consecutively or repetitively. Ginsenoside  $Rb_1$ , an active composition or component of the present invention is a sort of saponin, and can be formulated by the conventional methods. For example, the aqueous pharmaceutical composition of the present invention can be prepared as a preparation for intravenous administration by dissolving lyophilized ginsenoside  $Rb_1$  crystals or powders in physiological saline, distilled water, phosphate buffer or glucose solution. Lipid microspheres or liposome preparation can also be used. The concentrations of the pharmaceutical compositions comprising ginsenoside  $Rb_1$  or its salt in the preparations for intravenous administration can

optionally be adjusted unless so high, for example 0.01-10 mg/ml, preferably 0.1-1 mg/ml.

In the animal experiments of the present invention, ginsenoside  $Rb_1$  was intravenously administered continuously for 28 days after permanent occlusion of the cortical branch of the left middle cerebral artery (MCA). In the actual case of acute cerebral apoplexy, unless any treatment is given after the onset of cerebral apoplexy, rapid progress in cerebrovascular damage, slough and degeneration in the ischemic penumbra is noted within 2 weeks. As a result, the infarct lesion is expanded because the primary lesion as well as the secondary lesion (ischemic penumbra) becomes irreversible. Consequently, if ginsenoside  $Rb_1$  is administered during at least this period, it can be useful for the regeneration and reconstruction of vascular networks in the damaged ischemic penumbra and for suppression of the secondary lesion.

The present invention takes the initiative in addressing the regeneration and/or reconstruction of damaged and degenerated cerebral blood vessels by intravenous administration of ginsenoside  $Rb_1$ . The fact that ginsenoside  $Rb_1$  promotes cerebrovascular regeneration and reconstruction indicates that ginsenoside  $Rb_1$  is effective in promoting the regeneration and reconstruction of not only blood vessels of the nervous tissues but also those of the peripheral tissues.